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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,325	02/14/2002	Robert Bartlet Elliott	011115	3318

22876 7590 02/08/2005

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,325	ELLIOTT ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2004* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *110-114,116,117,120-123,125,152-211* is/are pending in the application.

4a) Of the above claim(s) *110-114,116,117,120-123,125,152-180,193 and 206-209* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *181-188,190,191,194-200,202-204,210 and 211* is/are rejected.

7)☒ Claim(s) *189,192,201 and 205* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/22/04 has been entered.

The amendment, Declaration under 37 CFR 1.131, and response submitted on 11/22/04 and 12/27/04 have been entered. Claims 118 and 124 have been canceled. Claims 110, 111, 116, 117, 123, 125, 152, 153, 155, 156 have been amended. Claims 157-211 are newly submitted.

It is noted that the amendments of claims 110, 152, 153 caused a shift of the invention from group I to group II as defined in the restriction requirement mailed 3/24/03. It is further noticed the newly submitted claims 157-180, 193, 206-209 also belong to group II of the inventions. Accordingly, Claims 110-114, 116, 117, 120-123, 125, 152-180, 193, 206-209 are withdrawn from consideration as drawn to non-elected invention. Claims 181-192, 194-205, 210-211 are under current examination. Since claims 181-192, 194-205, 210-211 are amended version of the original and subsequently presented claims 110-125 and 152-156, the standing rejections of

previous claims 110-114, 116, 117, 120-123, 125, 152-156 would apply to claims181-192, 194-205, and will be discussed in detail below.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 11/22/04 response would be addressed to the extent that they apply to current rejections.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of Claim 117, now new claims 191 and 203 respectively, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is withdrawn in view of claim amendment.

The previous rejection of Claim 117, now new claims 191 and 203 respectively, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, is withdrawn in view of claim amendment.

The previous rejection of claims 110, 116, and 118, under 35 U.S.C. 112, first paragraph, is withdrawn in view of the cancellation of claim 118, and its subject matter.

Claims 210 and 211 are rejected under 35U.S.C. 112 first paragraph, because the specification as originally filed does not describe the invention as now claimed. The original disclosure is completely silent regarding steps ii and iii of claim 210, thus the subject matter is now considered to be new matter.

The newly submitted claims 210 and 211 are drawn to transplanting non-encapsulated xenogenic porcine islet cells into a mammalian patient. However, the original disclosure only contemplates transplanting encapsulated porcine islet cells (e.g. Specification, page 6).

MPEP 2163.02 teaches that "WHENEVER THE ISSUE ARISES, THE FUNDAMENTAL FACTUAL INQUIRY IS WHETHER A CLAIM DEFINES AN INVENTION THAT IS CLEARLY CONVEYED TO THOSE SKILLED IN THE ART AT THE TIME THE APPLICATION WAS FILED...IF A CLAIM IS AMENDED TO INCLUDE SUBJECT MATTER, LIMITATIONS, OR TERMINOLOGY NOT PRESENT IN THE APPLICATION AS FILED, INVOLVING A DEPARTURE FROM, ADDITION TO, OR DELETION FROM THE DISCLOSURE OF THE APPLICATION AS FILED, THE EXAMINER SHOULD CONCLUDE THAT THE CLAIMED SUBJECT MATTER IS NOT DESCRIBED IN THAT APPLICATION". MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added). In the instant case, from

contemplating transplantation of encapsulated xenogenic cells to claiming implantation of un-encapsulated xenogenic cells is a clear addition or departure from the original disclosure. Accordingly, the amendment introduces new matter into the disclosure.

For reasons set forth above, the amendment filed 11/22/04 is objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention. Applicant is required to cancel the new matter in the reply to this Office Action. Alternatively, Applicant are invited to specifically point out where in the specification the support can be found for the amendment made to the disclosure.

To the extent that the claimed methods are not described in the instant disclosure, claims 210 and 211 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The prior rejection of Claims 110, 111, 120, 123 and newly submitted correspondent claims under 35 U.S.C. 102(e) as being anticipated by *Elliott* (6,146,653 or 6,090,400), and under 35 U.S.C. 102(f), are withdrawn in view of the declaration under 37 CFR § 1.132.

Claims 210 and 211 are rejected under 35 U.S.C. 102(e) as being anticipated by *Elliott* (USP 6,146,653 or 6,090,400).

Newly submitted claims 210 and 211 are drawn to treating a patient suffering from diabetes using xenogenic porcine islet as prepared by claim 181, and have overlapping scopes with claims 1-4, 6-8, 12 of the '400 patent, and claims 1-4, 6-8 of the '653 patent. Thus, the cited patents anticipate instant claims.

It is noted the applied references have a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome by an appropriate showing under 37 CFR 1.131.

Applicants are reminded that the declaration under 37 CFR § 1.132 cannot overcome a prior art rejection that claims the subject matter of the instant claims.

Claims 210 and 211 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. Claims 210 and 211 are directed to an invention not patentably distinct from claims 1-4 and 6-8 of commonly assigned USP 6,146,653 or 6,090,400. This rejection applies because there is no showing of common ownership *at time of applicant's invention.*

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned USP 6,146,653 or 6,090,400, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

In view of the amendment, Claim 181 and dependent claims, and claim 194 and dependent claims will be discussed separately as below.

It is noted that **claim 194** is a substantive equivalence of **previous claim 110 plus claim 120** (use of an islet trauma protecting agent), and obvious variants of previous claims 152 and 153. Thus the following rejections have the same reasoning as the previous correspondent rejections. They are modified only in the sense that the previous references addressing claim 120 drawn to the islet trauma protecting agent now become the references relied on to address the obviousness of the base claim 194.

The prior rejection of Claims 110, 111, 113, 120, 152-156 under 35 U.S.C. 103(a) as being obvious over *Rayat et al* (Diabetes 1998;47:1406-11), in view of *Nielsen et al* (US 6,225,310), and as evidenced by *Kallmann et al* (Life Sciences 1992;51;671-8) and *Elliott et al* (Ann N Y Acad Sci. 1993 Nov 30;696:333-41), now applies to claims 194, 195, 197.

The new claim 194 is the combination of previous claims 110 and 120, and obvious variation of previous claims 152 and 153. New claim 195 is a substantive equivalence of previous claim 111; and new claim 197 is a substantive equivalence of claim 113. The subject matter of these claims has been addressed in the previous Office action, and will not be reiterated.

The arguments presented in the 11/20/04 paper are drawn to amended claims 110, 111, 113, 120, 152-156 with a new limitation of encapsulation, these claims have been withdrawn from consideration, and thus the arguments drawn to encapsulation are moot. Accordingly, for reasons of record, the claimed invention remains obvious over *Rayat et al* in view of *Nielsen et al.*

The previous rejection of claim 112 under 35 U.S.C. 103(a) as being unpatentable over *Rayat et al* (Diabetes 1998;47:1406-11), and *Nielsen et al* (US 6,225,310) as applied to claims 110, 111, 113, 120, 152-156 above, and further in view of *Brandhorst et al* (Transplant 1999;68:355-61, IDS), now applies to claim 196, in addition to claims 194, 195, and 197.

Claim 196 is a substantive equivalence of previous claim 112, which has been addressed in the previous Office action, and will not be reiterated.

The arguments presented in the 11/22/04 paper are drawn to amended claims 110-113, 120, 152-156 with a new limitation of encapsulation, these claims have been withdrawn from consideration, and thus the arguments drawn to encapsulation are moot. Accordingly, for reasons of record, the claimed invention remains obvious over *Rayat et al* in view of *Nielsen et al* and *Brandhorst et al.*

The previous rejection of Claims 114, 116, 123 under 35 U.S.C. 103(a) as being unpatentable over *Rayat et al* (Diabetes 1998;47:1406-11) and *Nielsen et al* (US 6,225,310) as applied to claims 110, 111, 113, 120, 152-156 above, and further in view of *Clark et al* (Endocrinol 1990;126:1895-1903) and *Maysinger et al* (CA 2,216,055, IDS), now applies to claims 198 and 202, in addition to claims 194, 195, and 197.

Claims 198 and 202 are substantive equivalence of previous claims 114 and 116, which has been addressed in the previous Office action, and will not be reiterated.

The arguments presented in the 11/22/04 paper are drawn to amended claims 110, 111, 113, 114, 116, 120, 123,152-156, which have been withdrawn from consideration, and thus the arguments drawn to encapsulation are moot.

With respect to arguments concerning the reference of *Maysinger et al,* Applicants argue that *Maysinger et al* do not teach what was suggested by the Examiner, but rather *Maysinger et al* suggest that the decrease in beta cell mass following transplantation may be an effect of apoptosis in vivo. In response, Applicants'

attention is directed to the first sentence under § Summary of the Invention (page 4), which states, "ONE AIM OF THE PRESENT INVENTION IS TO PROVIDE A CULTURE MEDIUM WHICH PROMOTE ISLET CELL SURVIVAL", and "WHICH COMPRISES AT LEAST AN EFFECTIVE AMOUNT OF ONE OR MORE GROWTH FACTOR HAVING ANTI-APOPTOSIS EFFECT OF ISLET CELLS IN A PHYSIOLOGICALLY ACCEPTABLE CULTURE MEDIUM" (page 4, lines 25-28, emphasis added). In the preceding section, *Maysinger et al* discussed their observation, "WE HAVE ORIGINAL OBSERVATIONS ON HUMAN ISLETS AFTER ISOLATION. LIGHT MICROSCOPIC EXAMINATION OF THESE ISLETS JUST PRIOR TO CULTURE DEMONSTRATES THAT AT LEAST 15% OF THE CELLS HAVE MORPHOLOGICAL EVIDENCE OF APOPTOSIS" (page 3, lines 25-29), and concluded, "THESE DATA FORM THE BASIS FOR INVESTIGATING THE ROLE OF APOPTOSIS IN ISLET SURVIVAL AFTER ISOLATION" (page 4, lines 11-13, emphasis added). Evidently, *Maysinger et al* teach exactly what the Office suggests.

Accordingly, for reasons of record and set forth *supra*, the claimed invention remains obvious over *Rayat et al* in view of *Nielsen et al,* and further in view of *Clark et al* and *Maysinger et al.*

The previous rejection of Claims 116 and 117 under 35 U.S.C. 103(a) as being unpatentable over *Rayat et al* (Diabetes 1998;47:1406-11), *Nielsen et al* (US 6,225,310), *Clark et al* (Endocrinol 1990;126:1895-1903) and *Maysinger et al* (CA 2,216,055, IDS) as applied to claims 110, 113, 114, 116, 120, 123, 152-156 above, and further in view of *Saura et al* (Neuroendocrinol 1999 Jan 18;161-4); now applies to claims 202 and 203, in addition to claims 194, 195, 197, 198, 202.

Claims 202 and 203 are substantive equivalence of previous claims 116 and 117, which have been addressed in the previous Office action, and will not be reiterated.

The arguments presented in the 11/22/04 paper are drawn to amended claims 110-112, 114, 116, 117, 120, 152-156, which have been withdrawn from consideration, and thus the arguments drawn to encapsulation are moot.

With respect to the effect of IGF-1 vs. GPE, Applicants pointed to the specification reciting "improvements", and asserted that it is an unexpected beneficial results. In response, it is noted page 20 of the specification documented the results from static glucose stimulation of porcine islet cells after 3 days in culture, which indicated that with 0.01-1.0 μg/ml of GPE in culture (fig. 5), the insulin response to glucose increased up to about 1.8 fold compared to 1.5 fold when using the IGF-1 (Specification, page 18). This range of change (1.5 vs. 1.8) may well be standard variations among different experiments. Moreover, it could also be reasonably expected by the skilled in the art, because GPE is the functional unit of IGF-1, and a smaller molecule as taught by *Saura et al.* Thus, when using the same concentration, the medium containing GPE would have more functional units of IGF-1 than the medium containing the IGF-1. Thus, the skilled artisan would have a reasonable expectation of success following the teaching of *Saura et al* to reach the levels of improvement as disclosed in the specification. Further, the court has determined the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding *unexpected results*, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations

that the author(s) of the prior art derived the disclosed subject matter from the applicant. MPEP 716.01(c).

Accordingly, for reasons of record and set forth *supra*, the claimed invention remains obvious over *Rayat et al* in view of *Nielsen et al,* and further in view of *Clark et al*, *Maysinger et al,* and *Saura et al.*

The previous rejection of Claim 121 under 35 U.S.C. 103(a) as being unpatentable over *Rayat et al* (Diabetes 1998;47:1406-11) and *Nielsen et al* (US 6;225,310), as applied to claims 110, 111, 113, 120, 152-156 above, and further in view of *Pu et al* (Brit J Pharmacol 1996;118:1072-8), now applies to claims 199 and 200, in addition to claims 194, 195, and 197.

Claims 199 and 200 are encompassed by the previous claim 121, which has been addressed in the previous Office action, and will not be reiterated.

The arguments presented in the 11/22/04 paper are drawn to amended claims 110-112, 114, 120-122, 152-156, which have been withdrawn from consideration, and thus the arguments drawn to encapsulation are moot.

With respect to the argument that culturing the pig islets with lignocaine unexpectedly increased the viability of the pig islets by six-fold, it is persuasive with respect to claim 201. However, it is noted that claims 199 and 200 encompass any anesthetic agent, and any phospolipase A2 inhibitor, the alleged unexpected results do not apply to the broadly claimed agents. The court has determined, "WHETHER THE UNEXPECTED RESULTS ARE THE RESULT OF UNEXPECTEDLY IMPROVED RESULTS OR A PROPERTY NOT

TAUGHT BY THE PRIOR ART, THE "OBJECTIVE EVIDENCE OF NONOBVIOUSNESS MUST BE COMMENSURATE IN SCOPE WITH THE CLAIMS WHICH THE EVIDENCE IS OFFERED TO SUPPORT." IN OTHER WORDS, THE SHOWING OF UNEXPECTED RESULTS MUST BE REVIEWED TO SEE IF THE RESULTS OCCUR OVER THE ENTIRE CLAIMED RANGE. *IN RE CLEMENS*, 622 F.2D 1029, 1036, 206 USPQ 289, 296 (CCPA 1980)" ((MPEP 716.02(d), emphasis added)). Since the specification only discloses one agent out of the genus of anesthetic agents can achieve the unexpected results, the scope of the rejected claims are not commensurate in scope with the evidence offered. Accordingly, for reasons of record and set forth *supra*, the claimed invention remains obvious over *Rayat et al* in view of *Nielsen et al,* and further in view of *Pu et al.*

The previous rejection of Claim 124 under 35 U.S.C. 103(a) as being unpatentable over *Rayat et al* (Diabetes 1998;47:1406-11) and *Nielsen et al* (US 6,225,310), as applied to claims 110, 111, 113, 120, 152-156 above, and further in view of *Boss et al* (US 6,432,710) and *Champion et al* (US 4,850,993), now applies to claim 204, in addition to claims 194, 195, and 197.

Claim 204 is a substantive equivalence of the previous claim 124, which has been addressed in the previous Office action, and will not be reiterated.

The arguments presented in the 11/22/04 paper are drawn to amended claims 110, 111, 113, 120, 125, 152-156, which have been withdrawn from consideration, and thus the arguments drawn to encapsulation are moot.

With respect to argument that culturing pig islets with ciproxin unexpectedly increased the viability of the pig islets as shown in figure 4, it is persuasive with respect

to claim 205. However, it is noted that claims 194, 195, 197, 204 encompass any quinolone antibiotics, the alleged unexpected results do not apply to the broadly claimed genus of quinolone antibiotics. The court has determined, "WHETHER THE UNEXPECTED RESULTS ARE THE RESULT OF UNEXPECTEDLY IMPROVED RESULTS OR A PROPERTY NOT TAUGHT BY THE PRIOR ART, THE "OBJECTIVE EVIDENCE OF NONOBVIOUSNESS MUST BE COMMENSURATE IN SCOPE WITH THE CLAIMS WHICH THE EVIDENCE IS OFFERED TO SUPPORT." IN OTHER WORDS, THE SHOWING OF UNEXPECTED RESULTS MUST BE REVIEWED TO SEE IF THE RESULTS OCCUR OVER THE ENTIRE CLAIMED RANGE. *IN RE CLEMENS*, 622 F.2D 1029, 1036, 206 USPQ 289, 296 (CCPA 1980)" ((MPEP 716.02(d), emphasis added)). In this case, since the specification only discloses an unexpected results with ciprofloxacin and in light of applicants' argument, "*one of skill in the art would not have had a reasonable expectation that any antibiotic would affect insulin secretion from porcine islets*", nor would one of skill in the art have had a reasonable expectation that any antibiotic belong to the family of quinolone antibiotics would affect insulin secretion from porcine islets to the extend that an unexpected result would achieved as did ciprofloxacin.. The rejected claims are not commensurate in scope with the evidence offered to support. Accordingly, for reasons of record and set forth *supra*, the claimed invention remains obvious over *Rayat et al* in view of *Nielsen et al,* and further in view of *Boss et al*, and *Champion et al.*

It is noted that **claim 181** is a substantive equivalence of **previous claim 110 plus claim 124** (use of quinolone antibiotics), and obvious variants of previous claims 152 and 153. Thus the following rejections have the same reasoning as the previous rejections, they are modified only in the sense that the previous references addressing

claims 124 drawn to the use of quinolone antibiotics now become the references relied on to address the obviousness of the base claim 181.

The reasoning of the previous rejection of claims 110, 111, 113, 120, 124, 125, 152-156, applies to claims 181, 182, 184, 186, and will not be reiterated.

Claims 181, 182, 184, 186 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Rayat et al* (Diabetes 1998;47:1406-11) and *Nielsen et al* (US 6,225,310), and further in view of *Boss et al* (US 6,432,710) and *Champion et al* (US 4,850,993).

Claim 182 is a substantive equivalence of previous claim 111. Claim 184 is a substantive equivalence of previous claim 113. Claim 186 is a substantive equivalence of previous claim 120.

The arguments presented in the 11/22/04 paper are drawn to amended claims 110, 111, 113, 120, 124, 125, 152-156, which have been withdrawn from consideration, and thus the arguments drawn to encapsulation are moot.

With respect to the argument that culturing pig islets with ciproxin unexpectedly increased the viability of the pig islets as shown in figure 4, it is persuasive with respect to claim 192. However, it is noted that claims 181, 182, 184, 186 encompass any quinolone antibiotics, the alleged unexpected results do not apply to the broadly claimed genus of quinolone antibiotics. The court has determined, "WHETHER THE UNEXPECTED RESULTS ARE THE RESULT OF UNEXPECTEDLY IMPROVED RESULTS OR A PROPERTY NOT TAUGHT BY THE PRIOR ART, THE "OBJECTIVE EVIDENCE OF NONOBVIOUSNESS MUST BE COMMENSURATE IN SCOPE WITH THE CLAIMS WHICH THE EVIDENCE IS OFFERED TO SUPPORT." IN OTHER WORDS, THE

SHOWING OF UNEXPECTED RESULTS MUST BE REVIEWED TO SEE IF THE RESULTS OCCUR OVER THE ENTIRE CLAIMED RANGE. *IN RE CLEMENS*, 622 F.2D 1029, 1036, 206 USPQ 289, 296 (CCPA 1980)" ((MPEP 716.02(d), emphasis added)). In this case, since the specification only discloses an unexpected result of ciprofloxacin and in light of applicants' argument, "*one of skill in the art would not have had a reasonable expectation that any antibiotic would affect insulin secretion from porcine islets*", nor would one of skill in the art have had a reasonable expectation that any antibiotic that belong to the family of quinolone antibiotics would affect insulin secretion from porcine islets to the extend that an unexpected result would achieved as did ciprofloxacin. The rejected claims are not commensurate in scope with the evidence offered to support. Accordingly, for reasons of record and set forth *supra*, the claimed invention remains obvious over *Rayat et al* in view of *Nielsen et al,* and further in view of *Boss et al*, and *Champion et al.*

The reasoning of the previous rejection of claims 110, 111, 112, 113, 120, 124, 125, 152-156, applies to claim 181-184, 186, and will not be reiterated.

Claim 183 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Rayat et al* (Diabetes 1998;47:1406-11) in view of *Nielsen et al* (US 6,225,310), *Boss et al* (US 6,432,710) and *Champion et al* (US 4,850,993), as applied to claims 181, 182, 184, 186 above, and further in view of *Brandhorst et al* (Transplant 1999;68:355-61, IDS).

Claim 183 is a substantive equivalence of previous claim 112.

The arguments presented in the 11/22/04 paper are drawn to amended claims 110-113, 120, 124, 125,152-156, which have been withdrawn from consideration, and thus the arguments are moot.

Accordingly, for reasons of record and set forth *supra*, the claimed invention is obvious over *Rayat et al* in view of *Nielsen et al* and *Brandhorst et al.*

The reasoning of the previous rejection addressing claims 110, 111, 113, 114, 116, 120, 124, 125, 152-156, applies to claims 181, 182, 184-186, 190, and will not be reiterated.

Claims 185 and 190 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Rayat et al* (Diabetes 1998;47:1406-11) in view of *Nielsen et al* (US 6,225,310), *Boss et al* (US 6,432,710) and *Champion et al* (US 4,850,993), as applied to claims 181, 182, 184, 186 above, and further in view of *Clark et al* (Endocrinol 1990;126:1895-1903) and *Maysinger et al* (CA 2,216,055, IDS).

Claims 185 and 190 are substantive equivalence of previous claims 114 and 116, respectively.

The arguments presented in the 11/22/04 paper are drawn to amended claims 110, 111, 113, 120, 124, 125,152-156, which have been withdrawn from consideration, and thus the arguments drawn to encapsulation are moot.

With respect to arguments related to the reference of *Maysinger et al,* Applicants argue that *Maysinger et al* do not teach what was suggested by the Examiner, but rather *Maysinger et al* suggest that the decrease in beta cell mass following

transplantation may be an effect of apoptosis in vivo. In response, Applicants' attention is directed to the first sentence under § Summary of the Invention (page 4), which states, "ONE AIM OF THE PRESENT INVENTION IS TO PROVIDE A CULTURE MEDIUM WHICH PROMOTE ISLET CELL SURVIVAL", and "WHICH COMPRISES AT LEAST AN EFFECTIVE AMOUNT OF ONE OR MORE GROWTH FACTOR HAVING ANTI-APOPTOSIS EFFECT OF ISLET CELLS IN A PHYSIOLOGICALLY ACCEPTABLE CULTURE MEDIUM" (page 4, lines 25-28, emphasis added). In the preceding section, *Maysinger et al* discussed their observation, "WE HAVE ORIGINAL OBSERVATIONS ON HUMAN ISLETS AFTER ISOLATION. LIGHT MICROSCOPIC EXAMINATION OF THESE ISLETS JUST PRIOR TO CULTURE DEMONSTRATES THAT AT LEAST 15% OF THE CELLS HAVE MORPHOLOGICAL EVIDENCE OF APOPTOSIS" (page 3, lines 25-29), and concluded, "THESE DATA FORM THE BASIS FOR INVESTIGATING THE ROLE OF APOPTOSIS IN ISLET SURVIVAL AFTER ISOLATION" (page 4, lines 11-13, emphasis added). Evidently, *Maysinger et al* teach exactly what the Office suggests.

Accordingly, for reasons of record and set forth *supra*, the claimed invention remains obvious over *Rayat et al* in view of *Nielsen et al, Boss et al* and *Champion et al*, and further in view of *Clark et al* and *Maysinger et al.*

The reasoning of the previous rejection addressing claims 110, 111, 113, 120, 121, 124, 125, 152-156, applies to the following rejection, and will not be reiterated.

Claims 187 and 188 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Rayat et al* (Diabetes 1998;47:1406-11) in view of *Nielsen et al* (US 6,225,310), *Boss et al* (US 6,432,710), and *Champion et al* (US 4,850,993), as applied to claims 181, 182, 184, 186 above, and further in view of *Pu et al* (Brit J Pharmacol 1996;118:1072-8).

Claims 187 and 188 are encompassed by the previous claim 121.

The arguments presented in the 11/22/04 paper are drawn to amended claims 110, 111, 113, 120, 121, 124, 125, 152-156, which have been withdrawn from consideration, and thus arguments drawn to encapsulation are moot.

With respect to the argument that culturing the pig islets with lignocaine unexpectedly increased the viability of the pig islets by six-fold, it is persuasive with respect to claim 189. However, it is noted that claims 187 and 188 encompass any anaethetic agent, and any phospolipase A2 inhibitor, the alleged unexpected results do not apply to the broadly claimed agents. The court has determined, "WHETHER THE UNEXPECTED RESULTS ARE THE RESULT OF UNEXPECTEDLY IMPROVED RESULTS OR A PROPERTY NOT TAUGHT BY THE PRIOR ART, THE "OBJECTIVE EVIDENCE OF NONOBVIOUSNESS MUST BE COMMENSURATE IN SCOPE WITH THE CLAIMS WHICH THE EVIDENCE IS OFFERED TO SUPPORT." IN OTHER WORDS, THE SHOWING OF UNEXPECTED RESULTS MUST BE REVIEWED TO SEE IF THE RESULTS OCCUR OVER THE ENTIRE CLAIMED RANGE. *IN RE CLEMENS*, 622 F.2D 1029, 1036, 206 USPQ 289, 296 (CCPA 1980)" ((MPEP 716.02(d), emphasis added)). Since the specification only discloses one agent, out of the genus of anesthetic agents, can achieve the unexpected results, the scope of the rejected claims are not commensurate in scope with the evidence offered. Accordingly, for reasons of record and set forth *supra*, the claimed invention remains obvious over *Rayat et al* in view of *Nielsen et al, Boss et al* and *Champion et al*; and further in view of *Pu et al*.

The reasoning of the previous rejection addressing claims 110, 111, 113, 116, 117, 120, 124, 125, 152-156, applies to the following rejection, and will not be reiterated.

Claims 190 and 191 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Rayat et al* (Diabetes 1998;47:1406-11) in view of *Nielsen et al* (US 6,225,310), *Boss et al* (US 6,432,710), and *Champion et al* (US 4,850,993), as applied to claims 181, 182, 184, 186 above, and further in view of *Saura et al* (Neuroendocrinol 1999 Jan 18;161-4).

Claims 190 and 191 are substantive equivalence of the previous 116 and 117 respectively.

The arguments presented in the 11/22/04 paper are drawn to amended claims 110, 111, 113, 116, 117, 120, 124, 125, 152-156, which have been withdrawn from consideration, and thus arguments drawn to encapsulation are moot.

With respect to the effect of IGF-1 vs. GPE, Applicants pointed to the specification reciting "improvements", and asserted that it is an unexpected beneficial result. In response, it is noted page 20 of the specification documented the results from static glucose stimulation of porcine islet cells after 3 days in culture, which indicated that with 0.01-1.0 μg/ml of GPE in culture (fig. 5), the insulin response to glucose increased up to about 1.8 fold compared to 1.5 fold when using the IGF-1 (Specification, page 18). This range of change (1.5 vs. 1.8) may well be standard variations between experiments. Moreover, it could also be reasonably expected by the skilled in the art, because GPE is the functional unit of IGF-1, and a smaller molecule as taught by *Saura*

et al. Thus, when using the same weight/volume concentration, the medium containing GPE would have more functional units of IGF-1 than the medium containing the IGF-1. Thus, the skilled artisan would have a reasonable expectation of success following the teaching of *Saura et al* to reach the levels of improvement as disclosed in the specification. Further, the court has determined the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding *unexpected results*, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. MPEP 716.01(c).

Accordingly, for reasons of record and set forth *supra*, the claimed invention is obvious over *Rayat et al* in view of *Nielsen et al,* and further in view of *Clark et al, Maysinger et al,* and *Saura et al.*

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The previous rejection of claims 110, 111, 120, and 123 under the judicially created doctrine of obviousness-type double patenting now applies to new claims 194, 195, 197, 198, as being unpatentable over claims 11, 13, and 14 of U.S. Patent No. 6,146,653.

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 194, 195, 197, 198 of the present application are drawn to a method of preparing a xenotransplantable porcine islet comprising harvesting the pancreas of piglets from -20 to +10 days full term gestation, extracting pancreatic β islet cells, and exposing the islets to nicotinamide, whereas claims of the cited patent are drawn to a preparation of porcine islet cells for xenotransplantation prepared by the presently claimed method, which has been fully disclosed in the specification of the cited patent.

The claims of instant application and the cited patent differ in that claims of the cited patent are drawn to the product made by the instantly claimed method. However, there is no unobvious step in the processes, and the intended use of the method flows directly from the intended use recitation in the claims of the cited patent.

Accordingly, the claimed product and process in the cited patent and the present application are obvious variants. Therefore, the inventions as claimed are co-extensive.

In the 11/20/04 response, applicants' argument is drawn to claims of a different invention, which has been withdrawn from consideration, and thus the argument is moot.

Claims 210 and 211 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6-8 of U.S. Patent No. 6,146,653 and claims 1-4, 6-8, 12 of U.S. Patent No. 6,090,400.

Newly submitted claims 210 and 211 are drawn to treating a patient suffering from diabetes using porcine islet as prepared by claim 181 (correspondent to previous claim 110). Claims of the cited patents are drawn to treating diabetes with xenogenic porcine islet cells. Thus, Claims 210 and 211 have overlapping scopes with the claims of '400 and '653 patents.

Accordingly, the claims in the cited patents and the present application are obvious variants, and the inventions as claimed are co-extensive.

Claim Objections

Claims 189, 192, 201, 205 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Ram R. Shukla** can be reached on 571-272-0735. The fax numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Bus Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR

system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. Janice Li
Primary Examiner
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QL
February 7, 2005